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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,321	03/05/2001	Muralidhara Padigaru	15966-703 (Cura-203)	2997

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EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	19

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,321	PADIGARU ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,36,39 and 51-55* is/are pending in the application.

4a) Of the above claim(s) *51-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,36 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13, 14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Seq. Alignment* .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group II, claims 1-4, 36, and 39, drawn to SEQ ID NO:4 and pharmaceutical composition in Paper No. 17 is acknowledged.

Claims 51-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. This examiner notes that applicant requests joining of the new claims 51-55 along with the elected invention (method of making SEQ ID NO:4) under In Re Ochiai. Since the product claims are not allowed, the request for re-joining the product and process of making the product is denied. See claims rejections below. Claims 1-4, 36, 39, and 51-55 are pending and claims 1-4, 36, 39 are examined on merits.

Specification

The disclosure is objected to because it, for example at page 21,contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 36, and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a mature form" but it is not clear what the metes and bounds are for the phrase. What is the structural difference(s) between SEQ ID NO:4 and a mature form of SEQ ID NO:4?

Claim 1 recites "variant" but it is not clear what the metes and bounds are for the term.

Claim 4 recites "a conservative amino acid substitution" but it is not clear what the metes and bounds are for the phrase. The specification at page 113 the last paragraph does not define what is claimed for patent protection by reciting the limitation "a conservative amino acid substitution". The specification at page 113 the last paragraph says replacing non-essential amino acid of instant invention with a conservative amino acid, but the specification does not say which amino acids are essential and which is not.

Claims 1-4, 38, and 41 are confusing and indefinite because the claims are drawn to a mature form of SEQ ID NO:4, which the specification does not teach what it is. Therefore the limitation "15 %" difference from "a mature form" could read on many unrelated proteins.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 36, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, ***had possession*** of the claimed invention. The claims are drawn to a genus of proteins related to SEQ ID NO:4, with various differences in amino acid compositions from SEQ ID NO:4. The specification at page 10 (Table ID) discloses SEQ ID NO:4 (NOV1b protein) is a novel human 313-amino-acids protein. The claims, as written, however, encompass proteins which vary substantially in amino acid compositions and length. The instant specification provides an evidence for a single species of SEQ ID NO:4. Based on a single species, one cannot predict the types of additional species. Since the genus includes a large number of unpredictable species, possession of only one species is not seen as sufficient to reasonably convey

possession of the entire genus. It is concluded that applicant does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including other naturally occurring allelic variants.

Claim Rejections - 35 USC § 101

Claims 1-4, 36, and 39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Claims 1-4 are directed to SEQ ID NO:4, a novel human protein and variants of SEQ ID NO:4, with various differences in amino acid compositions from SEQ ID NO:4, claims 36 and 39 are drawn to pharmaceutical composition comprising proteins of claim 1 and a kit comprising said pharmaceutical composition.

The specification discloses that SEQ ID NO:4 is a newly identified protein and has homology to other human olfactory receptors. This disclosure is not sufficient to determine what the biological function(s) of SEQ ID NO:4 is because Scott et al (Nature Genetics, 1999, 21:440-443) teach that the function of newly identified gene products is unpredictable even when the database searches reveal significant homology to proteins of known function. Scott et al teaches that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter 'downregulated in adenoma'. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al. states that these results underscore the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al. (1990, Science 247:1306-1310) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted credible, specific and substantial utility of the newly identified instantly claimed protein and for the DNA molecule encoding the protein.

The specification contains assertions that the claimed invention, a novel human SEQ ID NO:4 polypeptide, antibody to SEQ ID NO:4, nucleic acid encoding SEQ ID NO:4 can be used for treatment and prevention of various human diseases listed at pages 16, 17, 149, and 150, 160. Other disclosed utilities are gene therapy (pages 37-42), antisense therapy (pages 60-64), making transgenic animals (pages 134-6), using as ingredients in pharmaceutical compositions (page 136-40), and detection, diagnosis and screening assays (pages 140-6,150-7), chromosome mapping (pages 146-8), and tissue typing (page 148-9), and others. These utilities are not specific to the claimed invention. The specification does not support a credible, specific and substantial utility because the specification does not teach a relationship to any specific disease or establish any involvement of the claimed invention in the etiology of any specific disease or does not teach what the function(s) of the protein is. There is no evidence in the specification that the various diseases listed at pages 16, 17, 149, and 150, 160 of the instant specification are caused by malfunction of the protein or can be treated by the instant invention. Also, the specification does not show whether the claimed polypeptide is overexpressed or underexpressed in a specific, diseased tissue compared to the healthy tissue control. Therefore, the disclosed utilities are not considered specific, credible, and substantial because they are just invitations for one skilled in the art to figure out how the protein functions or what the biological activities are for the claimed invention. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not how to find out how to use it for themselves. The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a credible, specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed protein. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

35 U.S.C. § 112, First Paragraph

Claims 1-4, 36, and 39 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know ***how to use*** the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 36, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Rouquier et al (IDS, March 18, 1998, Nat. Genet. 18, 243-250).

The claims are drawn to SEQ ID NO:4 and variants with various undefined structural similarities to SEQ ID NO:4, pharmaceutical comprising and a kit comprising the various proteins. Since claim 1 is drawn to polypeptides differ from 15 % or less from a mature form of SEQ ID NO:4 and the specification does not teach the identity of "a mature form", claims are interpreted as polypeptides having structural similarities to SEQ ID NO:4. Rouquier et al at Fig. 5 (at page 246) teach a polypeptide, which has 68.3 % identity to SEQ ID NO:4 (note the sequence alignment).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
October 22, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600